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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,489	02/26/2004	Samuel Zalipsky	ALZ5015 R1	7993

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EXAMINER	
SCHLIENTZ, LEAH H	
ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
05/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,489	ZALIPSKY ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-15 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-15 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 26 February 2004 and 17 October 2005 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

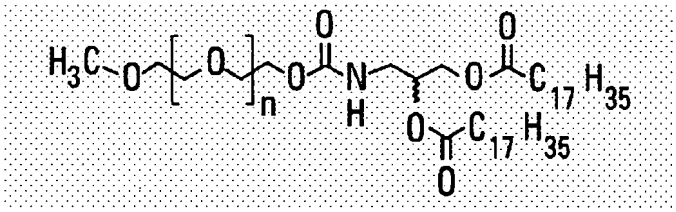
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 – 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Zalipsky (WO 01/05873).

Zalipsky discloses liposomes containing PEG-substituted neutral lipopolymers having the following structure:



The liposomes comprise about 1 – 10 mole percent of the PEG-substituted lipopolymers (claim 1). The PEG moiety of the lipopolymer compounds may be linked to a distearoyl moiety via a carbamate, ester, etc. linkage (page 3). The liposomes can be used to encapsulate a drug (page 6, lines 17 – 20). The liposomes are administered via injection (page 8). The circulation time of liposomes containing the PEG-substituted neutral lipopolymers is increased (claim 10).

It is noted that the Zalipsky does not specifically recite that the neutral lipopolymer-containing liposomes reduce liposome-induced complement activation upon

in vivo administration. However, because the same liposomes were administered as in the instantly claimed methods, such methods were inherently accomplished by Zalipsky upon administration of the liposomes to increase circulation time of the liposomes. The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make a claim patentable. See *In re Best,* 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977) and MPEP 2112. Provided that the only step that is required for reduction of complement activation is the administration of the liposomes, as claimed, Zalipsky administered the same liposomes and thus meets the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

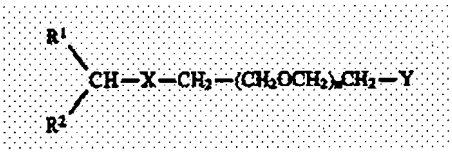
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 – 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zalipsky (WO 01/05873) in view of Watanabe (US 5,786,387).

Zalipsky discloses liposomes containing PEG-substituted neutral lipopolymers, as set forth above.

Zalipsky does not specifically teach that the drug which is encapsulated in the liposome is a chemotherapeutic agent.

Watanabe teaches a lipid double chain derivative containing a polyoxyethylene which is used as a fine particle drug carrier such as a mixed micelle or lipid emulsion or a liposome (column 1, lines 10 – 15). The lipid double chain derivative compound containing a PEO moiety has the following structure:



While it is noted that Watanabe teaches a variety of compounds, the compounds of Watanabe are the same as those of Zalipsky, for example, when R^1 is R^3-CO_2-CH_2—, R^2 is R^3CO_2— and R^3 is alkyl. X may be -CO-NH-, -CO-O-, -NH-CO-CH^2-O-, -CH_2-O-CO-CH_2-O-, etc. for, example, and Y may be alkoxy or hydroxyl (column 2, lines 15+). The compounds can be incorporated into liposomes and may be used as drug carriers (column 7, lines 34+). Drugs which can be carried include anticancer drugs, preferably adriamycin (i.e. doxorubicin) or methotrexate (column 8, lines 1 – 6).

Watanabe does not specifically teach that the liposomes comprise from 1 – 10 mole percent of the PEG-substituted lipopolymer compounds.

It would have been obvious to one of ordinary skill in the art to include anticancer drugs, such as adriamycin, methotrexate, etc. in the liposomes taught by Zalipsky who teaches that drugs are encapsulated in the liposomes. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so because Watanabe teaches that such anticancer drugs are capable of being encapsulated by liposomes comprising the same lipopolymers , and may be useful for cancer therapy. Both Zalipsky and Watanabe are drawn to PEGylated lipid derivatives and their incorporation into liposomes for the purposes of long circulation times in the blood.

It is noted that the Zalipsky does not specifically recite that the neutral lipopolymer-containing liposomes reduce liposome-induced complement activation upon *in vivo* administration. However, because the same liposomes were administered as in the instantly claimed methods, such methods were inherently accomplished by Zalipsky upon administration of the liposomes to increase circulation time of the liposomes. The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make a claim patentable. See *In re Best,* 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977) and MPEP 2112.

Claims 1 – 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zalipsky (WO 01/05873) in view of Watanabe (US 5,786,387), in further view of Abra *et al.* (US 5,945,122).

Zalipsky discloses liposomes containing PEG-substituted neutral lipopolymers, as set forth above.

Zalipsky does not specifically teach that the drug which is encapsulated is a chemotherapeutic agent.

Watanabe teaches lipid double chain derivative containing a polyoxyethylene which is used as a fine particle drug carrier such as in a liposome, wherein the drugs to be carried include anticancer agents, as set forth above.

Watanabe does not specifically recite cisplatin as the anticancer drug which is encapsulated.

Abra teaches a liposome composition containing an entrapped cisplatin compound (abstract). The liposomes are composed of a vesicle-forming lipid and between about 1-20 mole percent of a vesicle-forming lipid derivatized with a hydrophilic polymer (i.e. PEG) (column 2, lines 10 – 38). The cisplatin is entrapped with substantially greater retention in the liposomes when compared to liposomes lacking the polymer coating (abstract).

It would have been obvious to one of ordinary skill in the art to include anticancer drugs, such as adriamycin, methotrexate, etc. in the liposomes taught by Zalipsky who teaches that drugs are encapsulated in the liposomes. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so because Watanabe teaches that such anticancer drugs are capable of being encapsulated by liposomes comprising the same lipopolymers, and may be useful for cancer therapy. It would have been further obvious to include cisplatin as the anticancer drug which is encapsulated because Abra teaches that cisplatin is an anticancer drug which is difficult to encapsulate in liposomes because drug retention can be a problem, but that

encapsulation can be improved upon the incorporation of PEG into the liposome (abstract and column 1, line 63 – column 2, line 10). One would have been motivated to do, and would have had a reasonable expectation of success in doing so, because Zalipsky teaches that his liposomes provide advantages such as reduced leakage of an encapsulated cationic drug (page 6, line 18).

It is noted that the Zalipsky does not specifically recite that the neutral lipopolymer-containing liposomes reduce liposome-induced complement activation upon *in vivo* administration. However, because the same liposomes were administered as in the instantly claimed methods, such methods were inherently accomplished by Zalipsky upon administration of the liposomes to increase circulation time of the liposomes. The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make a claim patentable. See *In re Best,* 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977) and MPEP 2112.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LHS

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER